REMARKS

Claims 15, 17-20, 22, 24, 26, 27, 92, 94, 95, 97, 99-105, 107, 108, 110, 111, 113, 115, 116, 118 and 120 -161 are currently pending. Claims 1-14, 16, 21, 23, 25, 28-91, 93, 96, 98, 106, 109, 112, 114, 117 and 119 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of any or all of the canceled claims in one or more continuing applications.

Claims 122-161 are added. Support for these new claims can be found throughout the specification and claims as originally filed. For example, support for these claims can be found at original claims 1-28; at page 78, lines 1-31; at page 179, line 20 to page 183, line 17 and elsewhere throughout the specification as originally filed. Accordingly, new claims 122-161 do not add matter to the instant application.

After having carefully considered the final Office Action issued October 15, 2008 and the Advisory Action issued April 6, 2009, Applicants respectfully traverse the rejection of claims set forth therein.

Rejection of claims 15, 17-20, 22, 25, 26, 28, 92, 94, 96, 98-105, 107, 109, 110, 112, 113, 115, 117 and 119-121 under 35 U.S.C. § 112, first paragraph (written description)

In the final Office Action issued October 15, 2008, the Examiner rejected claims 15, 17-20, 22, 25, 26, 28, 92, 94, 96, 98-105, 107, 109, 110, 112, 113, 115, 117 and 119-121 under 35 U.S.C. § 112, first paragraph as allegedly not being supported by the specification. In particular, the Examiner asserted that recitation of "polypeptides having at least 95% sequence identity to SEQ ID NO: 3" and "polypeptides having at least 95% sequence identity to a chemokine-binding domain of SEQ ID NO: 3" in the above-rejected claims was not supported by the specification. In the response filed February 16, 2009, Applicants deleted the phrases "polypeptides having at least 95% sequence identity to SEQ ID NO: 3" and "polypeptides having at least 95% sequence identity to a chemokine-binding domain of SEQ ID NO: 3" from independent claims 15 and 101. In the Advisory Action issued April 6, 2009, the Examiner asserted that the independent claims could not be allowed unless they were further limited to recite that the chemokine-binding domain of SEQ ID NO: 3 "comprises the amino acid sequence 143-213 of SEQ ID NO: 3."

Applicants have not further amended independent claims 15 or 101 to include the limitation "comprises the amino acid sequence 143-213 of SEQ ID NO: 3." For at least the reasons set forth below, Applicants submit that independent claims 15 and 101, as well as each of the claims dependent thereon, are adequately supported by the specification.

Rejection of claims 15, 17-20, 22, 25, 26, 28, 92, 94, 96, 98-105, 107, 109, 110, 112, 113, 115, 117 and 119-121 under 35 U.S.C. § 112, first paragraph (enablement)

In the final Office Action issued October 15, 2008, the Examiner rejected claims 15, 17-20, 22, 25, 26, 28, 92, 94, 96, 98-105, 107, 109, 110, 112, 113, 115, 117 and 119-121 under 35 U.S.C. § 112, first paragraph as allegedly not being enabled by the specification. In particular, the Examiner asserted that methods of inhibiting chemokine activity and methods of chemokine binding that utilize "polypeptides having at least 95% sequence identity to SEQ ID NO: 3" and "polypeptides having at least 95% sequence identity to a chemokine-binding domain of SEQ ID NO: 3" were not enabled by the specification. In the response filed February 16, 2009, Applicants deleted the phrases "polypeptides having at least 95% sequence identity to SEQ ID NO: 3" and "polypeptides having at least 95% sequence identity to a chemokine-binding domain of SEQ ID NO: 3" from independent claims 15 and 101. In the Advisory Action issued April 6, 2009, the Examiner asserted that the independent claims could not be allowed unless they were further limited to recite that the chemokine-binding domain of SEQ ID NO: 3 "comprises the amino acid sequence 143-213 of SEQ ID NO: 3."

Applicants have not further amended independent claims 15 or 101 to include the limitation "comprises the amino acid sequence 143-213 of SEQ ID NO: 3." For the reasons set forth below, Applicants submit that independent claims 15 and 101, as well as each of the claims dependent thereon, are fully enabled by the specification.

The pending claims meet the requirements of 35 U.S.C. § 112

Applicants maintain the previously-filed claims without amendment. Additionally, Applicants have added new claims 122-161 in order to cover further aspects of the invention. For example, claims 122-141 are drawn to methods of inhibiting the activity of a chemokine using an agent comprising THAP 1 (SEQ ID NO: 3), a polypeptide having at least 95% sequence

identity to THAP1 (SEQ ID NO: 3), a chemokine-binding domain of THAP 1 (SEQ ID NO: 3) or a polypeptide having at least 95% sequence identity to a chemokine-binding domain of THAP1 (SEQ ID NO: 3). Claims 142-161 are drawn to methods of binding a chemokine using an agent comprising THAP1 (SEQ ID NO: 3), a polypeptide having at least 95% sequence identity to THAP1 (SEQ ID NO: 3), a chemokine-binding domain of THAP1 (SEQ ID NO: 3) or a polypeptide having at least 95% sequence identity to a chemokine-binding domain of THAP1 (SEQ ID NO: 3).

Applicants submit that the record shows that the instant specification provides adequate description and enablement for the subject matter claimed in each of the currently pending claims. As such, the arguments and remarks set forth in each of the responses previously filed in connection with the instant application are reiterated and incorporated herein by reference.

As discussed in the previously-filed responses, the instant specification describes what is meant by a chemokine-binding domain of SEQ ID NO: 3. A chemokine-binding domain is specifically described in the instant specification at page 181, line 21 to page 182, line 18. Moreover, as discussed further below, examples of deletion mutants and point mutants of SEQ ID NO: 3 that can and cannot bind chemokines are described in Figure 12 of the specification.

In addition to the foregoing, as discussed in the previously-filed responses, the specification describes amino acid sequences having at least 95% amino acid identity with SEQ ID NO: 3 or a chemokine-binding domain of SEQ ID NO: 3. An example of a general description of sequence identity is found in the instant specification at page 78, lines 1-31. Polypeptides having at least 95% amino acid sequence identity with SEQ ID NO: 3 that bind to chemokines and inhibit chemokine activity are also particularly identified in the specification. For example, Figure 12 of the instant specification shows a first mutant having at least 95% amino acid sequence identity with SEQ ID NO: 3 (arginine residues at positions 171 and 172 converted to alanines) can still bind the chemokine, SLC, while a second mutant having at least 95% amino acid sequence identity with SEQ ID NO: 3 (deletion of the amino acids residues 168-172), does not bind SLC. Figure 12 also shows that the full-length SEQ ID NO: 3 and at least three different N-terminal deletion mutants of SEQ ID NO: 3 can bind to chemokine SLC. Elsewhere, the instant specification describes over 100 THAP polypeptide sequences and domains from humans and other animals that have varying degrees of amino acid sequence

identity with that of SEQ ID NO: 3 or a chemokine-binding domain of SEQ ID NO: 3 (see Figure 9 of the instant specification).

In view of the foregoing remarks, Applicants respectfully submit that the specification provides a representative number of polypeptides that include a chemokine-binding domain of THAP1 (SEQ ID NO: 3), that have at least 95% amino acid sequence identity with THAP1 (SEQ ID NO: 3) and that have at least 95% amino acid sequence identity with a chemokine-binding domain of THAP1 (SEQ ID NO: 3).

It is also clear that the specification describes most, if not all, of the chemokines known at the time of filing the instant application as being used in the claimed methods. For example, at page 115, lines 4-26, the specification clearly states that:

> In some embodiments of the present invention, THAP-type chemokine-binding agents bind to or otherwise modulate the activity of one or more chemokines selected from the group consisting of XCL1, XCL2, CCL1, CCL2, CCL3, CCL3L1, SCYA3L2, CCL4, CCL4L, CCL5, CCL6, CCL7, CCL8, SCYA9, SCYA10, CCL11, SCYA12, CCL13, CCL14, CCL15, CCL16, CCL17, CCL18, CCL19, CCL20, CCL21, CCL22, CCL23, CCL24, CCL25, CCL26, CCL27, CCL28, clone 391, CARP CC-1, CCL1, CK-1, regakine-1, K203, CXCL1, CXCL1P, CXCL2, CXCL3, PF4, PF4V1, CXCL5, CXCL6, PPBP, SPBPBP, IL8, CXCL9, CXCL10, CXCL11, CXCL12, CXCL14, CXCL15, CXCL16, NAP-4, LFCA-1, Scyba, JSC, VHSV-induced protein, CX3CL1, and fCL1.
> (page 115, lines 4-26).

Additionally, the specification exemplifies methods of binding and/or inhibiting the activity for a representative number of chemokines. At the time of filing the instant application, there were only about 65 known chemokines. Approximately 27 CCL family chemokines and about 14 CXCL family chemokines were known. The specification provides specific examples of binding and/or inhibiting the activity for three chemokines of the CCL family and two chemokines of the CXCL family. As such, the specification describes methods of binding and

inhibiting the activity of a representative number of chemokines from each of the major families of chemokines.

In addition to the foregoing, the instant specification enables a skilled artisan to determine other variants of THAP1 (SEQ ID NO: 3) or chemokine-binding domains of THAP1 (SEQ ID NO: 3) that can bind to and/or inhibit the activity of chemokines using only routine experimentation. As discussed above, the specification describes THAP1 polypeptides and THAP1 chemokine-binding domains from numerous organisms as well as polypeptides having at least 95% amino acid identity to THAP1 or having at least 95% amino acid identity to a chemokine-binding domain of THAP1. For non-naturally occurring THAP1 and THAP1 chemokine-binding domain homologs, the specification describes routine preparation methods using well known deletion and mutagenesis methods (see page 99, line 23 to page 107, line 32).

In addition to the foregoing teachings, the specification provides working examples (Examples 15-17, 32 and 33), that demonstrate how to test the binding of chemokines to full-length THAP1, chemokine-binding domains of THAP1, polypeptides having at least 95% amino acid identity to THAP1 and polypeptides having at least 95% amino acid identity to a chemokine-binding domain of THAP1. Specifically, these working examples show that THAP1 and homologs thereof, as well as the chemokine-binding domain of THAP1 and homologs thereof, bind to various chemokines, including CCL21, CCL19, CCL5, CXCL9 and CXCL10 (see Figures 12 and 19). Generally, these examples describe routine procedures that one of ordinary skill in the art can use to determine whether any THAP1 polypeptide, polypeptide having at least 95% amino acid identity to THAP1, chemokine-binding domain of THAP1 and/or polypeptide having at least 95% amino acid identity to a chemokine-binding domain of THAP1, including the polypeptides described in the specification, binds to one or more chemokines. Indeed, Applicants have used these very methods to determine the specificity of chemokine binding to the chemokine-binding domains of human THAP2 and human THAP3 (see Example 38 and Figures 21A-E and 22A-C of U.S. Patent Application No. 11/360,450, which claims priority to the instant application).

Assays for determining the effect of THAP1, chemokine-binding domains of THAP1, polypeptides having at least 95% amino acid identity to THAP1 and polypeptides having at least 95% amino acid identity to a chemokine-binding domain of THAP1 on chemokine activity are

described in Examples 34-37. Again, Applicants have used these routine methods to demonstrate that that such polypeptides inhibit the chemokine activity in both *in vitro* and *in vivo* assays (see Examples 41-43 of U.S. Patent Application No. 11/360,450, which claims priority to the instant application).

Finally, Applicants have also previously provided a Declaration of Dr. Jean-Philippe Girard, which describes experiments that we performed essentially according to the methods set forth in Examples 34-36 of the instant application. In these experiments, it was demonstrated that constructs comprising a chemokine-binding domain of THAP1 could inhibit the activity of chemokine CCL5 *in vivo*. In view of the guidance set out in the specification, as skilled artisan could easily determine each and every chemokine that is bound by or inhibited by THAP1, a chemokine-binding domain of THAP1, polypeptides having at least 95% amino acid identity to THAP1 and polypeptides having at least 95% amino acid identity to a chemokine-binding domain of THAP1.

Applicants would like to remind the Examiner that undue experimentation is not measured by the amount of time, expense or quantity of routine experimentation that is involved in implementing the disclosed methods. (see *In re Wands* 858 F.2d 731 (Fed. Cir. 1988); *United States v. Telectronics Inc.*, 857 F.2d 778 (Fed. Cir. 1998); and M.P.E.P. § 2164.06). Provided that the procedure used to implement the claimed invention is routine, it is of little consequence to enablement the number of iterations or the length of the procedure that is required before the end is achieved. As described above, Applicants have provided detailed guidance describing how to obtain THAP1 polypeptides, polypeptides having at least 95% amino acid identity to THAP1, chemokine-binding domains of THAP1 and polypeptides having at least 95% amino acid identity to a chemokine-binding domain of THAP1, and further how to test these polypeptides to determine their ability bind chemokines and inhibit chemokine activity. All of the methods used to obtain and test these polypeptides are known in the art and fully described in the specification. As such, only routine experimentation is required to determine which additional THAP1 polypeptides, polypeptides having at least 95% amino acid identity to THAP1, chemokine-binding domains of THAP1 and polypeptides having at least 95% amino acid identity to a chemokine-binding domain of THAP1 inhibit the activity of one or more chemokines.

In view of the foregoing remarks, Applicants respectfully submit that the specification enables a skilled artisan to fully practice the invention as set forth in the claims using no more than routine experimentation.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. However, if any issues remain Applicants request that the Examiner contact the undersigned in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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